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# B Upper Respiratory Tract Infections

# 58 The Common Cold

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## SHORT VIEW SUMMARY

**Definition**
- The common cold is an upper respiratory illness that includes rhinorrhea and nasal obstruction as prominent symptoms.

**Epidemiology**
- Common cold illnesses occur 5 to 7 times per year in children and 2 to 3 times per year in adults.
- Illnesses occur most commonly between the early fall and late spring in temperate climates.
- Transmission of the viral pathogens causing the common cold may occur via direct contact, large-particle aerosol, or small-particle aerosol.

**Microbiology**
- The rhinoviruses are responsible for the majority of common cold illnesses.
- Coronavirus, respiratory syncytial virus, and metapneumovirus may also be associated with the common cold syndrome.
- Other respiratory viruses may cause common cold symptoms, but are frequently associated with lower respiratory symptoms in addition to the upper respiratory illness.
- Coinfection with more than one pathogen is common in these illnesses.

**Diagnosis**
- The diagnosis of the common cold is a clinical diagnosis.
- The responsible pathogen(s) can be determined by polymerase chain reaction assay, but this is rarely useful in the management of the patient.

**Therapy**
- There are no specific antiviral agents that are useful for treatment of the common cold.
- Management depends on symptomatic therapy with treatment directed at the most bothersome symptoms.

**Prevention**
- There are no proven interventions for prevention of the common cold.

The term *common cold* refers to a syndrome of upper respiratory symptoms that may be caused by a variety of viral pathogens. References to these illnesses in ancient writings attest to the long association of colds and human health. Early observers noted that colds waned in frequency during sea voyages and then reappeared when social contact was reestablished, suggesting that these illnesses were transmitted from person to person. This observation was confirmed in human transmission studies conducted in the early 20th century. These studies established that transmission of colds was due to a "filterable agent" present in nasal secretions.[1] Epidemiologic studies begun by Dingle and co-workers[2] in the 1940s, among families in Cleveland, demonstrated the role of the family in the spread of colds and emphasized the greater incidence among children than adults. The pathogens responsible for the common cold syndrome were not identified, however, until the development of cell culture systems for detection of viral infections.

The clinical significance of the common cold derives primarily from the frequency of these illnesses in the general population. Although generally mild and self-limited, these illnesses are associated with an enormous economic burden both in lost productivity and in expenditures for treatment. Viral respiratory tract infection accounts for approximately 21 million days of school absence and 20 million days of work absence in the United States annually.[3] Each year there are approximately 110 million physician visits, and patients purchase almost $3 billion worth of over-the-counter cough and cold medications for treatment of common cold symptoms.[4] In recent years, particularly since the widespread use of the polymerase chain reaction (PCR) for detection of viral pathogens, there has been an increasing appreciation of the morbidity associated with the common cold viruses and the complications of these illnesses.

## ETIOLOGY

The pathogens most frequently associated with common cold symptoms are the rhinoviruses that cause approximately half of all colds (Table 58-1). Other important pathogens include the coronaviruses and respiratory syncytial virus (RSV). Influenza, parainfluenza, and adenoviruses may be associated with cold symptoms; however, these agents frequently cause lower respiratory or systemic symptoms in addition to the upper respiratory symptoms characteristic of the common cold. Recent data suggest that the prevalence of different viruses may be different in an urban compared with a suburban environment.[5]

Knowledge of the pathogens associated with the common cold is based primarily on studies that relied on cell culture isolation for detection of virus. Systematic studies of common cold epidemiology using more sensitive diagnostic methods have not been done, although studies using PCR techniques in selected study populations and over limited time periods have generally confirmed the cell culture findings.[6] The use of the more sensitive techniques, however, has permitted detection and characterization of previously unrecognized pathogens. Metapneumovirus, first detected in 2001, appears to be the cause of approximately 5% of common cold illnesses (see Chapter 161).[7,8] Bocavirus, a human parvovirus discovered in respiratory secretions in 2005, has since been detected in a small proportion (≈5%) of children with respiratory disease (see Chapter 149).[9,10] This virus is frequently detected in patients who are coinfected with previously recognized respiratory pathogens or who are asymptomatic; thus, the role of bocavirus as a common cold pathogen has not been established.[11,12] The use of PCR assay has also revealed that coinfection by multiple viral pathogens is frequent during a common cold illness.[13,14]

## EPIDEMIOLOGY

### Seasonal Incidence

In temperate climates, colds occur year-round but have a decreased incidence during the summer months. The "respiratory virus season" in the northern hemisphere begins with an increase in rhinovirus infections in August or September and ends after the spring peak of rhinovirus infections in April or May.[15-17] Although rhinovirus continues to circulate at lower levels throughout the winter months, the

**KEYWORDS**
antihistamine; antitussive; coronavirus; decongestant; *Echinacea;* metapneumovirus; respiratory syncytial virus; rhinovirus; zinc

**TABLE 58-1 Viruses Associated with the Common Cold**

| VIRUS GROUP | ANTIGENIC TYPES | PERCENTAGE OF CASES |
|---|---|---|
| Rhinoviruses | >100 types | 40-50 |
| Coronaviruses | 5 types | 10-15 |
| Parainfluenza virus | 5 types | 5 |
| Respiratory syncytial virus | 2 types | 5 |
| Influenza virus | 3 types* | 25-30 |
| Adenovirus | 57 types | 5-10 |
| Metapneumovirus | 2 types | 5 |
| Other viruses: enteroviruses, bocavirus | | |

*Multiple subtypes.

season bracketed by these rhinovirus peaks consists of sequential and relatively discrete outbreaks caused by different viral pathogens.[16,18] The seasonal incidence for parainfluenza viruses usually peaks late in the fall and late in the spring, and for RSV and influenza viruses, it is highest between December and April.[16,19] An increased incidence of common cold symptoms is associated with each of these outbreaks. However, pathogens other than rhinovirus or coronavirus are generally associated with the occurrence in the community of other clinical syndromes, such as croup or bronchiolitis, that are more characteristic of an epidemic pathogen. In tropical climates, the common cold is prevalent throughout the year, and the incidence has little correlation to climatic changes, although outbreaks of influenza and parainfluenza may be associated with rainy seasons.[20,21]

### Attack Rate

The average incidence of the common cold in preschool children is 5 to 7 per year but 10% to 15% of children will have at least 12 infections per year.[2,22,23] The incidence of illness decreases with age and averages 2 to 3 per year by adulthood. The incidence of common colds is increased by contact with children in the home or extensive contact with children outside the home, as in child care centers. Children cared for in out-of-home daycare centers during the first year of life have 50% more colds than children cared for only at home.[24-26] The difference in the incidence of illness between these groups of children decreases as the length of time spent in daycare increases. However, the incidence of illness remains higher in the daycare group through at least the first 3 years of life.[25]

### Transmission

In general, respiratory viruses are spread by three mechanisms: small-particle aerosols, large-particle aerosols, and direct contact.[27] Small-particle aerosols form droplet nuclei that do not settle and can be transmitted over relatively long distances by airflow. When inhaled, these aerosols may reach the lower airway. Large-particle aerosols refer to droplets generated from the airway that settle rapidly and are transmitted only over relatively short distances. These particles are generally filtered by the upper respiratory tract and are not deposited in the lower respiratory tract. Direct contact refers to contact with contaminated fomites as well as direct person-to-person contact. Studies of experimental and natural rhinovirus colds in human volunteers suggest that transmission may occur by both direct contact and by large-particle aerosols.[28,29] The transmission of the other pathogens associated with colds is less well studied. RSV appears to require close contact for spread and, under experimental conditions, has been spread by direct contact with contaminated fomites.[30] In contrast to rhinovirus and RSV, influenza appears to spread from person to person predominantly by small-particle aerosols.[31] Regardless of the mechanism of transmission, initiation of a common cold illness requires that the pathogen come in contact with, and infect, the nasal epithelium.

### Immunity and Factors Predisposing to Infection or Illness

Infection with the respiratory viruses reliably produces an adaptive immune response. The risk of infection on subsequent exposure to the virus appears to be related to the presence or absence of specific antibody to the pathogen. The frequency of infection with these viruses is due to the various mechanisms that the pathogens have evolved to avoid host defenses. Infections with rhinoviruses and adenoviruses result in the development of serotype-specific protective immunity. Repeated infections with these pathogens occur because there are a large number of distinct serotypes of each virus (see Table 58-1). Similarly, the influenza viruses behave as though there were multiple virus serotypes, by virtue of the changes of the antigens presented on the surface of the virus. The interaction of coronaviruses with host immunity is not well defined, but it appears that there are multiple distinct strains of coronavirus that are capable of inducing at least short-term protective immunity.[32] In contrast, the parainfluenza viruses, metapneumovirus, and RSV each have a small number of distinct serotypes. Reinfection with these viruses occurs because complete protective immunity to these pathogens does not develop after an infection. Although reinfection is not prevented by the adaptive host response to these viruses, the risk of infection is decreased, and the severity of subsequent illness is moderated by preexisting immunity.

A number of putative interventions for prevention of the common cold claim to act by enhancing or supporting nonspecific immune function. Despite these claims, there is no evidence that nonspecific depression of immune function plays any role in the risk of acquisition of infection or the severity of illness. Several studies have suggested that genetic polymorphisms that result in decreased concentrations of mannose-binding lectin may increase susceptibility to viral respiratory infection, particularly in young children.[33,34] The data are not conclusive, however, and the importance of polymorphisms in this component of the innate immune system remains to be determined.[35]

The effect of personality and stress on infection and illness associated with upper respiratory pathogens has also been evaluated. These studies suggest that stress is not a factor in the acquisition of infection but that chronic stress, in particular, is associated with the development of more severe symptoms.[36] Personality type may also impact symptom severity. Introverted individuals are reported to have more severe illness.[37] In contrast, a positive emotional style, characterized by a general attitude of vigor and well-being, is associated with a reduction in symptom severity.[38]

## PATHOGENESIS

Viral infection of the nasal epithelium may be associated with destruction of the epithelial lining, as with influenza viruses and adenoviruses; less extensive effects, as with coronavirus 229E;[39] or there may be no apparent histologic damage, as with rhinoviruses and RSV. Regardless of the histopathologic findings, infection of the nasal epithelium is associated with an acute inflammatory response characterized by release of a variety of inflammatory cytokines and infiltration of the mucosa by inflammatory cells. Although there is some variation in the specific pathways involved in the response to the different viral pathogens, this acute inflammatory response appears to be responsible, at least in part, for many of the symptoms associated with the common cold.

Information about the pathogenesis of specific symptoms of the common cold is limited. Nasal obstruction and rhinorrhea are the prominent symptoms of the cold. The nasal inflammatory response appears to be associated with pooling of blood in the capacitance vessels of the nose and increased nasal blood flow.[40] The important contribution of these changes to nasal obstruction is demonstrated by the substantial decongestant effect associated with the use of topical vasoconstrictors.[41] Increased vascular permeability with leakage of serum into the nasal mucosa and nasal secretions may also contribute to nasal obstruction.[42-44] Transudation of serum into the secretions is a major contributor to rhinorrhea early in the course of the cold.[42-44] The contribution of glandular secretions from the nose to rhinorrhea becomes more important later in the course of the illness.[43]

Cough is a less common symptom in colds, but when it occurs, it is frequently reported as the most bothersome symptom. The pathogenesis of cough in colds is poorly understood and may be due to a variety of different mechanisms. Extension of viral infection into the lower respiratory tract appears to be associated with cough in some patients.[45] There is also evidence that in some patients cough is

triggered by neural reflexes as a result of stimulation of sensitized upper airway receptors.[46,47] Throat irritation associated with postnasal drip may be associated with voluntary "throat-clearing" that appears to be a distinct mechanism of cough.[48]

The sore throat that is characteristic of rhinovirus colds may be produced by elaboration of bradykinin as a part of the inflammatory response. Increased concentrations of bradykinin are found in nasal secretions during rhinovirus colds, and challenge of normal volunteers with bradykinin produces sore throat symptoms.[49,50]

## CLINICAL MANIFESTATIONS

The onset of common cold symptoms typically occurs 1 to 3 days after viral infection.[51] The first symptom noted is frequently a sore or "scratchy" throat, followed closely by nasal obstruction and rhinorrhea. The sore throat usually resolves quickly, and by the second and third day of illness, nasal symptoms predominate. Cough is associated with approximately 30% of colds and usually begins after the onset of nasal symptoms. Systemic symptoms are uncommon in colds, but influenza viruses, RSV, and adenoviruses are more likely than are rhinoviruses or coronaviruses to be associated with fever and other constitutional symptoms. The usual cold persists about 1 week, although 25% last 2 weeks.[52,53] Recent data suggest that coinfection by multiple pathogens may be associated with prolonged illnesses.[13] Virus shedding persists after the resolution of symptoms, and virus may be cultured from 10% to 20% of subjects for 2 to 3 weeks after infection.[54,55]

The physical findings of the common cold are limited to the upper respiratory tract. Increased nasal secretion is frequently obvious to the examiner. A change in the color or consistency of the secretions is common during the course of the illness and is not indicative of sinusitis or bacterial superinfection. Examination of the nasal cavity may reveal swollen, erythematous nasal turbinates, although this finding is nonspecific and of limited diagnostic usefulness.

## DIFFERENTIAL DIAGNOSIS

The most important task of the physician caring for a patient with a cold is to exclude other conditions that are potentially more serious or treatable. The differential diagnosis of the common cold includes noninfectious disorders as well as other upper respiratory tract infections (URIs). Allergic rhinitis has a similar symptom complex to the common cold. The presence of nasal or conjunctival itching suggests allergic disease, and some data suggest that patients can reliably differentiate these illnesses.[56] Other less common causes of upper respiratory symptoms are a foreign body, streptococcosis, and the catarrhal phase of pertussis. Sinusitis may occur acutely or as a complication of the common cold. Sinus involvement is present in uncomplicated common cold illnesses and, most commonly, does not indicate a superimposed bacterial infection. Bacterial sinusitis may be difficult to differentiate.[57,58] Bacterial sinusitis is more likely to be present if symptoms persist for more than 10 days, if severe illness is present, or if symptoms worsen after improvement (see Chapter 63).[59,60]

## LABORATORY FINDINGS

Routine laboratory studies are not helpful for the diagnosis and management of the common cold. A nasal smear for eosinophils may be useful if allergic rhinitis is suspected. A predominance of polymorphonuclear leukocytes in nasal secretions is characteristic of uncomplicated colds and does not indicate bacterial superinfection.

The viral pathogens associated with the common cold may be detected by culture, antigen detection, PCR, or serologic methods. These studies are not generally indicated in patients with colds because a specific etiologic diagnosis is useful only when treatment with an antiviral agent is contemplated. Bacterial cultures or antigen detection is useful only when group A streptococcus, *Bordetella pertussis*, or nasal diphtheria is suspected. The isolation of other bacterial pathogens is not an indication of bacterial nasal infection and is not a specific predictor of the etiologic agent in sinusitis.

## COMPLICATIONS OF THE COMMON COLD

Although the common cold generally has little medical significance, a recent study found that acute otitis media was diagnosed in association with 30% of viral URIs.[14,61] Sinusitis was associated with 8% of viral URIs.[61] These complications may be a direct result of the viral infection or may be due to bacterial superinfection. Viral RNA was detected by PCR assay in the middle ear fluid of 44 (48%) of 91 patients with acute otitis media.[62] In 25 (57%) of these patients, there was concurrent isolation of a bacterial pathogen in the middle ear fluid. Similarly, rhinovirus was detected in sinus brushings of 8 (40%) of 20 adult patients with maxillary sinusitis.[63]

## THERAPY

Specific antiviral therapy is not currently available for the treatment of common cold illnesses. The neuraminidase inhibitors oseltamivir and zanamivir have a modest effect on the duration of symptoms associated with influenza virus infections. The difficulty of distinguishing influenza from other common cold pathogens and the necessity that therapy be started early in the illness are practical limitations to the use of these agents for mild URIs. Antibacterial therapy is of no benefit in the treatment of the common cold.

### Symptomatic Therapies

The current treatment of the common cold relies on symptomatic remedies directed at specific symptoms. For common colds, the efficacy of treatments for nasal obstruction, rhinorrhea, and the pain symptoms (i.e., sore throat and headache) has been demonstrated in studies done in adults (Table 58-2). Attempts to demonstrate beneficial effects of these agents in children have failed, although it is not clear whether this failure is due to a lack of effect in children or simply due to the difficulty in assessing subjective symptoms in this population. Given the absence of demonstrated benefit and the potential for toxicity, symptomatic common cold therapies are not recommended for children younger than 4 years.

### Nasal Congestion

Both topical and oral adrenergic agents are effective nasal decongestants.[41,64-66] Comparative studies have not been done regarding the common cold. However, it is generally accepted that the topical agents are more potent than the oral drugs.[67] Prolonged use of the topical adrenergic agents should be avoided to prevent the development of rhinitis medicamentosa, an apparent rebound effect when the drug is discontinued. Systemic absorption of the imidazolines (e.g., oxymetazoline and xylometazoline) has been associated, rarely, with bradycardia, hypotension, and coma. The systemic side effects of the oral adrenergic agents are central nervous system stimulation, hypertension, and palpitations. The antihistamines have no effect on nasal congestion.

### Rhinorrhea

The treatment of rhinorrhea is primarily by blockade of cholinergic stimulation of glandular secretion. Atropine or ipratropium bromide treatment of experimental rhinovirus colds produced a small decrease in rhinorrhea, or nasal mucus weights, that was not statistically significant.[68,69] In larger studies of subjects with natural colds, ipratropium produced a 22% to 31% decrease in rhinorrhea compared with placebo.[70-72] Ipratropium has been approved for use for the treatment of rhinorrhea in the common cold. The most common side effects of intranasal ipratropium are nasal irritation and bleeding.

The first-generation antihistamines have been used for many years for treatment of rhinorrhea associated with the common cold. A

**TABLE 58-2 Effective Treatments for Symptoms of the Common Cold**

| SYMPTOM | TREATMENT |
|---|---|
| Nasal obstruction | Topical adrenergic agents, oral adrenergic agents |
| Rhinorrhea | First-generation antihistamines, ipratropium bromide |
| Sneezing | First-generation antihistamines |
| Sore throat | Acetaminophen, ibuprofen, and other NSAIDs |
| Cough | First-generation antihistamines; bronchodilators (?) |

NSAIDs, nonsteroidal anti-inflammatory drugs.

modest but statistically significant effect on rhinorrhea has been found in several small studies in adults, although other studies have failed to detect any therapeutic effect.[73-76] A large study in experimental colds found that clemastine fumarate reduced rhinorrhea by approximately 27% compared with placebo.[77] This observation was subsequently confirmed in a natural cold trial.[78] The second-generation or "nonsedating" antihistamines have had no effect on common cold symptoms in a limited number of studies.[79-81] This observation, the absence of histamine in the secretions of most subjects with colds, and the similarity of the response to ipratropium and the antihistamines, suggest that the effect of the antihistamines on rhinorrhea is related to the anticholinergic rather than the antihistaminic properties of these drugs. The major side effect associated with the use of the antihistamines is sedation and drying of the eyes, mouth, and nose.

### Sneezing

Sneezing is frequently reported as a symptom during the common cold; however, it is rarely considered the most bothersome symptom by the patient. The antihistamines are effective for treatment of sneezing.[76-78]

### Sore Throat

Sore throat is a common symptom early in the course of the cold and is frequently the first symptom noticed by the patient. The sore throat associated with colds is generally not severe and is often described as a "scratchy throat." Treatment with mild analgesics is occasionally indicated, particularly if there is associated myalgia or headache.

### Cough

Cough during colds is produced by several different mechanisms, and treatment should be directed at the most likely underlying cause. Cough in some patients appears to be due to nasal obstruction or postnasal drip. Cough in these patients is most prominent during the time of greatest nasal symptoms and may respond to treatment with a throat-soothing demulcent, such as honey, or an antihistamine or antihistamine/decongestant combination.[82-84] In other patients, cough may be a result of virus-induced reactive airway disease or to viral infection of the lower airways.[45,47,85] These patients may have cough that persists for days to weeks after the acute illness and may benefit from bronchodilator therapy. Cough that persists after the resolution of other cold symptoms or that persists in association with unremitting rhinorrhea may be due to sinusitis and may respond to antibiotic therapy.[86] Nonspecific cough suppression with either codeine or dextromethorphan hydrobromide is frequently used; however, the efficacy of these agents has not been demonstrated in the common cold.[87,88] A single study has described a modest effect of nonsteroidal anti-inflammatory drugs (NSAIDs) on the acute cough of colds.[89] Expectorants such as guaifenesin are not effective antitussive agents.[90]

### Other Remedies

(Also see Chapter 50.)

Virtually everyone has experienced the common cold. Colds are self-limiting, vary in severity from episode to episode, and have an unpredictable incidence over time, providing a fertile environment for anecdotal reports of putative preventatives and remedies. Many different, nonconventional remedies have been promoted, but few have been subjected to rigorous scientific evaluation.

A potential role for zinc as a treatment for the common cold was first suggested by the observation that zinc is an inhibitor of rhinovirus 3C protease, an enzyme essential for virus replication.[91,92] Although zinc has never been shown to have a significant antiviral effect in vivo, this observation produced numerous clinical trials to evaluate the effectiveness of zinc as a common cold therapy. The results of these studies range from dramatic reductions in common cold severity to no detectable effect.[93] The studies that found no effect of zinc have been criticized as having small sample sizes, for using inadequate doses of zinc, or for using formulations of zinc that might inactivate the zinc salts. The studies reporting a significant effect of zinc have been criticized for inadequate blinding either by the use of poorly matched placebos, or because the active preparation was associated with a high incidence of adverse effects. Studies in the experimental rhinovirus colds model have consistently shown either no or relatively modest treatment effects of zinc preparations on common cold illness.[94-96] The uncertain treatment effects of zinc must also be viewed in light of the side effects of this treatment. Oral zinc lozenges may be associated with a sore mouth and occasional nausea. Intranasal zinc may cause nasal irritation and has been anecdotally linked to anosmia.

*Echinacea* is a traditional remedy for the common cold, and the use of this herb for treatment of respiratory symptoms dates to the late 1800s. There are three species of *Echinacea* with different phytochemical characteristics that are used for medicinal purposes. The phytochemical composition of *Echinacea* preparations may also vary because of differences in the part of the plant used, the type of extraction, and even the geographic location and time of year the plant is harvested. Despite the differences in the *Echinacea* preparations, only recently have there been attempts to standardize and characterize the material used in clinical trials. Many studies of *Echinacea* prevention or treatment of the common cold have been reported, but the lack of characterization of the product and inattention to careful study design limit the interpretation and generalizability of the results.[97,98] Although early studies suggested that *Echinacea* may have beneficial treatment effects, recent, more rigorous studies have failed to find any effect of *Echinacea* on common cold symptoms.[99,100] Given the variation in *Echinacea* products, the possibility that *Echinacea* preparations with different phytochemical profiles might be beneficial cannot be excluded. The accumulating evidence, however, suggests that it is prudent to assume that *Echinacea* has no beneficial effect until positive evidence of a treatment effect is produced.

## PREVENTION

Chemoprophylaxis or immunoprophylaxis is generally not available for the common cold. Immunization or chemoprophylaxis against influenza may be useful for prevention of colds caused by this pathogen; however, influenza is responsible for only a small proportion of all colds. Nonpharmacologic interventions touted as effective prophylaxis for the common cold include zinc; vitamins C, D, and E; *Echinacea;* ginseng; exercise; and hand hygiene. Unfortunately, when these interventions have been subjected to rigorous evaluation, evidence for effectiveness has not been found.[99,101-103] Hand hygiene and exercise have undeniable benefits for health in general and can be recommended despite the paucity of evidence specific to common cold prevention. The other interventions, although apparently safe, have no demonstrable benefit and simply contribute to the unnecessary health care expenditures related to the common cold.

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*The complete reference list is available online at Expert Consult.*


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